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Malnutrition is Associated With Fatigue and Anxiety in Advanced Cancer Patients Admitted to Home Palliative Care

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Sebastiano Mercadante, MD[1,2], Giuseppe Massimo Bellavia, MD[1], Flavio Fusco, MD[3], Lucia Adamoli, MD[1], Carla Scibilia, MD[1], Alessio Lo Cascio, RN[2], and Alessandra Casuccio, MSc[4]

Abstract

Objective: Information regarding the nutrition profile of advanced cancer patients followed at home is lacking. The aim of this study was to assess the nutritional status of patients who were admitted to specialized home palliative care, and examine eventual factors associated with malnutrition. **Design:** Cross-sectional. Setting/subject: patients who were admitted to 2 specialized home palliative care programs. **Participants:** A consecutive sample of patients admitted to home care was selected. Depression, anxiety, nausea, poor appetite, and poor well-being were measured by numerical scale 0-10. Mini nutritional assessment form (MNA-SF), fatigue assessment scale (FAS), and sarcopenia by SARC-F. were performed. The use of drugs used for anorexia, including corticosteroids, progestins, or others, was recorded. **Results:** Data of 135 patients were analyzed. Sixty-eight per cent and 77% of patients resulted to be malnourished and sarcopenic. In the multivariate regression analysis, anxiety ($P = 0.036$) and total FAS ($P = 0.013$) were independently associated with malnutrition. Fifty-five per cent of patients were receiving corticosteroids or megestol acetate. No significant associations with parameters examined were found. **Conclusion:** The majority of advanced cancer patients admitted to home palliative care were malnourished independently of the primary tumor diagnosis. Indeed, fatigue and anxiety were independently associated with malnutrition.

Keywords

malnutrition, sarcopenia, advanced cancer, palliative care, home care

Key-messages

1. This study reported that a large number of patients admitted to specialized home palliative care are malnourished and sarcopenic.
2. Anxiety and fatigue were independently associated with malnutrition
3. This study suggests to systematically assess the nutritional status and evaluate the need for an intervention on individual basis, according to expected survival

Introduction

About 18 million new cancer patients and 9.6 million cancer-related deaths occurred in 2018 worldwide. Many of these patients are living longer with metastatic disease due to advances in diagnostics and treatments.[1] Patients with severe, progressive, and incurable diseases, such as advanced cancer, should receive palliative care to improve quality of life through prevention and relief of suffering, pain, and other physical, psychosocial, and spiritual manifestations.[2] Palliative care in incurable cancer should be focused on symptom control, especially those impacting nutrition, and initiated simultaneously with active care at diagnosis since patients identify malnutrition as the primary cause of physical, cognitive, and social function loss.[3] It has been suggested that advanced cancer patients receiving palliative care should be assessed for nutritional deficiencies. Regardless of whether they are still on anticancer treatments or not, in these patients

[1]Regional Home Palliative Care Program, SAMOT, Palermo, Italy
[2]Main Regional Center for Supportive and Palliative Care, La Maddalena Cancer Center, Palermo, Italy
[3]Palliative Care Unit, ASL3 Liguria, Genua, Italy
[4]University of Palermo, Palermo, Italy

Corresponding Author:
Sebastiano Mercadante, MD, Pain Relief & Palliative Care Unit, La Maddalena Cancer Center, Via San Lorenzo 312, Palermo 90146, Italy.
Email: terapiadeldolore@lamaddalenanet.it

malnutrition leads to low performance status, impaired quality of life, unplanned hospitalizations, and reduced survival.[4]

The role of nutritional support for cancer patients in palliative care is still a controversial issue.[5] In a recent review, the prevalence of weight loss and associated symptoms was quite heterogeneous. There was a large range of variability influenced by age and social factors, comorbidities, and setting of care. The advanced stage was found to be linked to a higher risk of developing malnutrition, as an expression of the relationship between tumor burden, inflammatory status, reduced caloric intake, and malabsorption.[6]

Advanced cancer patients spend most time at home. The importance of providing optimal palliative care that supports patients with advanced illness and caregivers who wish to stay at home is of paramount importance. Clear benefits of home palliative care in helping patients to die at home with reduced symptom burden and without impacting on caregiver grief have been reported, particularly those with advanced cancer.[7] This suggests providing home palliative care for patients who wish to die at home.

Information regarding the nutritional status of advanced cancer patients admitted to home palliative care is lacking. Given the relevance of assessing nutritional and functional aspects of palliative care and the lack of studies addressing the topic, this study aimed to investigate the nutrition profile of advanced cancer patients who were admitted to specialized home palliative care.

Methods

This was a cross-sectional study of patients who were admitted to 2 specialized home palliative care program in Italy, in Palermo and Genua. A group of home care physicians adhered to the protocol and were trained to use of the tools selected for this study, with the help of a dietician. A consecutive sample of advanced cancer patients at admission of home care was assessed for a period of 6 months. Inclusion criteria were: age >18 years and advanced cancer disease. Exclusion criteria were: refusal of informed consent, expected survival less than 1 week, cognitive failure or incapacity to help assessment, and language barriers.

Epidemiological data was recorded, including age, gender, primary diagnosis, and Karnofsky level. Items of Edmonton Symptom Assessment Scale including depression, anxiety, nausea, poor appetite, and poor well-being were measured. The following parameters were assessed: mini nutritional assessment form (MNA-SF), fatigue assessment scale (FAS), and the SARC-F. The MNA-SF is a screening tool to help identify patients who are malnourished or at risk of malnutrition. It consists of 6 items: decline in food intake, weight loss, mobility, psychological stress or acute disease, neuropsychological problems, and the BMI. The scale is scored out of a total of 14 points and values below a threshold of 12 were used to identify patients at risk. The range 8-11 points corresponds to risk of malnutrition, while patients with 0-7 points are considered malnourished.[8] FAS is a validated tool, which has psychometric properties. Each item is scored on a 5-point scale from 1 (never) to 5 (always)[9]; total scores range from 10 to 50.[8] We examined the presence/absence of clinically significant fatigue by dichotomizing the scale at the validated threshold: no fatigue (scores of 10-21) vs fatigue (scores of 22-50).[10] SARC-F is a clinical index for sarcopenia screening. It includes 5 components: aid for walking, falls, getting up from a chair, climbing stairs, and strength. The scores for each item range from zero to 2, obtaining a total score between zero to 10 points. A score greater than or equal to 4 is defined as risk of sarcopenia.[11] Drugs used for anorexia, including corticosteroids, progestins, or others, were recorded, and when available, laboratory data. Patient's informed consent and local ethical committee approval were obtained.

Statistical Analysis

Absolute and relative frequencies have been reported for qualitative variables, and means and standard deviation (SD) for quantitative variables. Frequency analysis was performed using the Pearson's chi-square test and Fisher exact test, as needed. An univariate and multivariable regression model was used to examine the correlations between malnutrition patient status (dependent variables), and clinical patient characteristics (independent variables). Odds ratios and related 95% confidence intervals (95% CI) were reported as well as the *P*-value. Data were analyzed by IBM SPSS Software 24 version (IBM Corp., Armonk, NY, USA). All *P*-values were two-sided and $P \leq 0.05$ was considered statistically significant.

Results

Three-hundred-forty-three patients were consecutively assessed. Two-hundred-eight patients were not considered, according to the exclusion criteria: language barriers (n.8), no informed consent (n.13), poor prognosis-not collaborating (n.187).

Data of 135 patients were assessed. The principal characteristics of patients and parameters recorded are reported in Table 1. The mean age was 75.6 SD ± 10.6), 75 patients were males, and mean Karnofsky status ±was 40.5 (SD ± 10.2).

Almost all patients were no longer receiving anticancer therapy

Nine-two patients were malnourished (68%) and 35 were at risk of malnutrition (26%) (MNA-SF ≤7 and <12, respectively). One-hundred-four patients (77%) had sarcopenia (SARC-F ≥4).

At univariate analysis, age ($P = 0.015$), Karnofsky ($P = 0.001$), depression ($P = 0.005$), anxiety ($P = 0.008$), poor appetite ($P = 0.031$), poor well-being ($P = 0.006$), total FAS ($P = 0.001$), and total SARC-F ($P < 0.0005$) were significantly associated with malnutrition. In the multivariate regression analysis, anxiety (OR 2.849, 95% CI 1.070-7.591; $P = 0.036$)

Table 1. Principal Characteristics and Data of Patients Admitted to Home Care.

Age (mean, SD)	75.6 (10.6)
Gender (m/f)	75/60
Karnofsky (mean, SD)	40.5 (10.2)
Primary tumor (n°)	135
Gastrointestinal	53
Lung	40
Urogenital	14
Hematologic	13
Breast	6
Head and neck	6
Other	3
Depression	4.3 (2.7)
Anxiety	4.3 (2.9)
Nausea	1.8 (2.6)
Poor appetite	4.7 (2.6)
Poor well-being	5.5 (2.4)
MNA-SF (mean, SD)	6.4 (3.0)
FAS (mean, SD)	29.7 (7.6)
SARC-F (mean, SD)	5.8 (2.6)

and total FAS (OR: 1.693 (95%CI 1.116-2.566; $P = 0.013$) were independently associated with malnutrition.

Seventy-five patients were receiving corticosteroids or megestol acetate. No significant associations with parameters examined were found.

Discussion

This study reported the data regarding the nutritional status of advanced cancer patients admitted to home care. About 68% of patients were malnourished, and 77% were sarcopenic. There was an independent correlation between malnutrition and fatigue measured with FAS. Of interest, anxiety was independently associated with malnutrition. While psychological symptoms invariably belong to the cluster of poor appetite, nausea, weakness, or poor-well-being,[12-16] nutritional status has not been taken into consideration.

No differences among primary tumors was found. Pancreatic, eosphageal, gastroenteric cancers, head and neck and lung cancer have been reported to be more likely associated with malnutrition.[6] This finding could be attributed to the very advanced stage of disease, flatting any difference among tumors, or may be due to the low number of patients in each tumor category.

Many patients were receiving drugs that are commonly used for a variety of symptoms other than improving appetite. The use of corticosteroids for the cluster of symptoms including, fatigue, lack of appetite, anorexia-cachexia, and well-being, remains controversial, as their efficacy may vary depending on the patients' general condition and seems to be reduced in patients with advanced stage of disease or poor performance status.[17] Corticosteroids and progestins have been found to have the potential to offer some benefit.[18] Recently, efficacy of corticosteroids for cancer-related cachexia was reported to be less relevant[16] than that reported in previous randomized controlled trials.[19,20] Given the cross-sectional design of this study it is difficult to draw information regarding the effect of these drugs in a population with a limited survival at time of admission to home palliative care. These agents are, however, associated with potentially substantial systemic side effects including electrolyte disturbances, cardiovascular effects, diabetes mellitus and loss of bone density and osteoporosis with concomitant vertebral fracture. It is widely accepted that aggressive feeding interventions are not appropriate at the end of life, and weight loss and reduced food intake are inevitable part of the dying process.[21-25] In a recent opinion expert paper, it has been reported that any form of clinical assisted nutrition is primarily indicated for the prevention of death from malnutrition in selected individuals from specific groups of patients with advanced cancer, for patients with an inability to introduce sufficient nutrients, and/or an inability to digest sufficient nutrients, but not indicated for the management of anorexia, weight loss, cancer cachexia, or reduced oral intake due to nutrition impact symptoms.[26]

Data regarding nutritional assessment of advanced cancer patients admitted to home palliative care is poor, and prevalently based on the use of parenteral nutrition[27-30] or performed at home with cancer and non-cancer diseases,[29] or in other palliative care settings, namely inpatient units.[31-33] Malnutrition and poor quality of life are prevalent among advanced cancer patients in home palliative care. In a small study with a cross-sectional design in patients receiving home palliative care, 52.5% of patients were moderately or suspected of being malnourished and 32.8% of them were severely malnourished. Patient-Generated Subjective Global Assessment (PG-SGA) score used in this study showed a lower total quality of life, psychophysiological well-being, functional well-being and social/spiritual well-being.[34] In a cross-sectional multicenter Spanish study performed in different settings including oncology, radiotherapy, and home palliative care, more than 50% of patients had moderate-severe malnutrition, assessed by PG-SGA.[35] It is likely that in home palliative care patients, malnutrition rate would be higher, although this distinction among the settings was not reported.

Patients with advanced cancer are commonly more malnourished compared to cancer patients in earlier stages.[36] In this study, where patients with poor immediate prognosis were excluded, survival was, however, relatively short, mostly in the range of 2-3 months, considering the large range of an advanced cancer status, which can be 6-24 months.[4] Eating has also a symbolic meaning, other than providing some pleasure. Patients with advanced cancer have differing preferences for living with eating-related

concerns. Preferences range from acceptance to engaging in self-action. Change in eating habits is often of concern to patients with advanced cancer. Some patients were found to live with their eating troubles by engaging in self-action and expressed concern about lack of support for this behavior. Eating-related concerns are challenging for supporting differing patient preferences for living with the symptom, which can include the expectation of support for self-action.

There are some limitations of this study, such as the large number of excluded patients. This limitation is frequently reported in studies of palliative care patients in the late stage of disease. Another limitation was the lack of monitoring of nutrient intake in these patients at this stage of disease for finding possible correlations with malnutrition, FAS, and SARC. Finally, the study lacks longitudinal assessment, having a cross-sectional evaluation at time of admission to home palliative care. However, this information may be useful for understanding the frequency of malnutrition in this population and to plan further studies regarding the best strategy for these patients.

Conclusion

The majority of advanced cancer patients admitted to home palliative care are malnourished independently of the primary tumor diagnosis. Indeed, fatigue and anxiety were independently associated with malnutrition. Longitudinal studies may help to provide more information about these relationships. More studies should afford the question whether active treatments with orexant drugs or nutritional supplements may have a role in the comprehensive palliative care management to improve quality of life of very advanced cancer patients with a short survival time followed at home.

Author Contributions

SM: Conceptualization; AL: Data curation; Supervision, writing original draft. AC; Formal analysis; GB Methodologly. FF, GB, LA, CS; Investigation; All: Writing - review & editing.

Declaration of Conflicting Interests

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Authorship

SM: project, protocol, analysis, writing. GMB: recruiting; FF: recruiting; LA; recruiting; CS: recruiting; ALC: data manager. AC: statistical analysis. All authors approved the final paper.

Ethical Statement

Ethical Approval

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Ethical committee of Palermo.

Informed Consent

Written informed consent was obtained from all subjects/patients.

ORCID iD

Sebastiano Mercadante https://orcid.org/0000-0001-9859-6487

Data Availability Statement

Data available on request.*

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